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LXXVIII.—*Examination of the Bark of Croton gubouga.*
Isolation of 4-Hydroxyhygric Acid.

By JOHN AUGUSTUS GOODSON and HUBERT WILLIAM BENTLEY
CLEWER.

Croton gubouga, S. Moore, is a small tree growing on the low veldt in the Eastern Transvaal near the Sabi and Selati rivers. The bark of the tree has a considerable local reputation among the natives as a remedy for malaria, and both the seeds and the bark have been used by Captain Maberley in conjunction with opium in the treatment of malarial fever (*Lancet*, 1899, 157, 874).

A preliminary examination of the bark and the seeds has been made by Mr. H. H. Green, B.Sc., in South Africa (private communication), who found that the ground bark caused purgation and emesis in dogs, but that rabbits were less sensitive to its action, although in doses of 1 gram per kilogram of body-weight it induced diarrhoea. In human beings administration of the bark according to Mr. Green causes an intense burning sensation in the throat, salivation, and slight nausea, with, in some cases, a slight laxative effect. The seeds exert a similar action. Mr. Green further observed that the acrid substance to which these effects are ascribed is extracted to some extent by hot water, and readily by ether.

The bark has also been examined by Greenish (*Pharm. J.*, 1918, 101, 289), who found that the acrid constituent was largely extracted by hot light petroleum as well as by ether, chloroform, or alcohol.

For the material used in the present investigation the authors are indebted to Mr. I. B. Pole Evans, Chief of the Division of Botany, Union of South Africa.

The bark had a slight but not unpleasant odour. Dust from the ground bark caused sneezing and produced a burning sensation in the throat and on the tongue. It has not been possible to isolate the acrid constituent to which the irritant properties of the bark are due, in a form suitable for investigation, and it is possible that the seeds, which it is hoped to examine shortly, may prove more suitable for this purpose. The present paper deals chiefly with an acid isolated from the bark, which has proved to be a new optically active hydroxyhygric acid.

Preliminary Examination.

When extracted with Prollius' fluid the ground bark yielded a trace of alkaloid and furnished the following percentages of extract when exhausted in a Soxhlet apparatus with solvents in the order named: petroleum (b. p. 35—60°), 3; ether, 0·7; chloroform, 0·3; ethyl acetate, 0·8; alcohol, 4·3; total, 9·1.

Petroleum Extract.—This extract, on treatment with ether, left only a trace of insoluble matter. The solution yielded only traces of material to aqueous solutions of ammonium and potassium carbonates, but potassium hydroxide solution extracted a quantity of brown potassium salt, from which fatty acids (A), equivalent to 21 per cent. of the original extract, were recovered.

The solution left after the removal of the fatty acids contains the acrid constituent of the bark, but the authors have not yet been able to isolate this in a condition suitable for investigation (compare Greenish, *loc. cit.*). Hydrolysis, by alkalis, as described below, destroyed this acrid constituent.

The neutral material was hydrolysed by boiling for one hour with potassium hydroxide in alcoholic solution, after which the solution was concentrated, mixed with water, and extracted with ether to remove unsaponifiable matter. This, amounting to 20 per cent. of the original extract, included only a trace of hydrocarbon, or higher aliphatic alcohol, and consisted of semi-solid matter, from which a phytosterol was isolated, which gave a well-marked Liebermann reaction and on acetylation yielded a substance melting at 117°, probably a mixture of acetyl derivatives.

The remaining alkaline liquid was acidified with sulphuric acid, and the mixture distilled in a current of steam, when a yield of about 3·4 per cent. of volatile acids was obtained. The distillate was dissolved in an excess of barium hydroxide solution, the excess of baryta removed by carbon dioxide, and the filtrate concentrated. On adding silver nitrate solution to this liquid, silver was immediately precipitated; moreover, the solution instantly decolorised permanganate, indicating the presence of formic acid. On further concentration a quantity of a sparingly soluble barium salt separated. This was removed and converted into the acid, which was then dissolved in a slight excess of sodium hydroxide, and a silver salt prepared:

0·0413 gave 0·0178 Ag. $\text{Ag} = 43\cdot1$.

$\text{C}_8\text{H}_{15}\text{O}_2\text{Ag}$ (silver *n*-octoate) requires $\text{Ag} = 43\cdot0$ per cent.

The aqueous solution of the barium salts from which the above-described acid was separated still contained formic acid, and in

order to remove it, the solution was acidified, shaken with ether, and the ethereal solution well washed with water. In this way a further quantity of acid was obtained, which was fractionally converted into silver salts and the five fractions obtained were analysed:

1. 0.1315 gave 0.0665 Ag. Ag=50.6.
2. 0.1817 „ 0.0934 Ag. Ag=51.4.
3. 0.1448 „ 0.0744 Ag. Ag=51.4.
4. 0.0951 „ 0.0490 Ag. Ag=51.5.
5. 0.0273 „ 0.0141 Ag. Ag=51.7.

$C_5H_9O_2Ag$ (silver valerate) requires Ag=51.6 per cent.

The volatile acids present in the plant appear, therefore, to include formic, valeric, and *n*-octoic acids.

The acid liquid which had been distilled in a current of steam was extracted with ether, and the dark-coloured residue digested twice with petroleum. This left undissolved a dark-coloured, amorphous, resinous substance. The solution when concentrated gave a 23 per cent. yield of fatty acids, which were mixed with the 21 per cent. of free acids (*A*) previously obtained (see above). The acids were converted into lead salts, which from their behaviour appeared to be a mixture of lead salts of saturated and unsaturated fatty acids.

Ethereal Extract.—This consisted of a dark green resin, which on digestion with ether left a quantity of a light coloured substance undissolved. This was almost insoluble in the usual organic solvents except pyridine, from a dilute solution in which it separated in microscopic crystals melting at about 250° and giving the Liebermann reaction, whence it appeared to be a phytosterolin. The ethereal solution was then extracted first with water, removing about 10 per cent. of the extract, and finally with potassium hydroxide solution, which extracted 36 per cent. of acidic resin, leaving neutral resin; none of these yielded any crystalline material.

Chloroform and Ethyl Acetate Extracts.—These extracts consisted of amorphous resins. From the chloroform extract there separated gradually a fawn-coloured material, which was not obtained crystalline, nor could a crystalline acetyl derivative be prepared from it.

Alcoholic Extract.—This extract was redissolved in alcohol and water added, which precipitated a quantity of a nearly black tar. The clear liquid was treated with an excess of basic lead acetate, the precipitate filtered off, and the lead removed from the precipitate and filtrate by means of hydrogen sulphide in the usual way. The concentrated liquid from the former gave a nearly black colour with

ferric chloride and contained tannin. The concentrated filtrate was evaporated to complete dryness, and finally digested on the water-bath with nine successive portions of about 50 c.c. each of absolute alcohol to separate the large quantity of reducing sugars present. Each fraction was poured from the syrupy residue while hot, and when cold, again poured from a small amount of separated syrup, which was returned to the larger bulk. Crystals separated from each fraction when kept, but only a small quantity from the last. The whole amount of crystalline matter accumulated weighed about 6 grams. This substance proved to be 4-hydroxyhygric acid, an optically active acid not previously described.

Examination of the Acid.

To obtain sufficient material for the identification of the acid, further quantities of the bark were extracted, when the following varying percentage yields were obtained: 0.41, 0.21, and 0.25, amounting in all to 16.35 grams of crude acid.

The product may be readily purified by boiling its solution in water with animal charcoal, repeatedly concentrating the filtrate under diminished pressure with additions of alcohol, until the pure acid separates from the hot solution in colourless needles or prisms, which contain varying amounts of water of crystallisation, thus:

I. 0.1986 lost 0.0170 at 110°. $\text{H}_2\text{O} = 8.56$.

II. 0.2108 ,, 0.0108 ,, 110°. $\text{H}_2\text{O} = 5.13$.

Although the acid is very readily soluble in water it may be crystallised from that solvent. 7.05 Grams of substance were dissolved in water, and the solution was concentrated until about 4.5 grams of water remained. The solution was seeded and allowed to remain overnight, when 1.25 grams of the acid had separated in crystals, which appeared to be truncated prisms. These crystals, after being dried in the air, were found to contain one molecule of water:

0.2035 lost 0.0220 at 110°. $\text{H}_2\text{O} = 10.8$.

$\text{C}_6\text{H}_{11}\text{O}_3\text{N} \cdot \text{H}_2\text{O}$ requires $\text{H}_2\text{O} = 11.0$ per cent.

I. 0.1324 * gave 0.2402 CO_2 and 0.0938 H_2O . $\text{C} = 49.5$; $\text{H} = 7.9$.

II. 0.1090 * ,, 0.1976 CO_2 ,, 0.0778 H_2O . $\text{C} = 49.5$; $\text{H} = 8.0$.

0.1474 gave 12.6 c.c. N_2 at 17° and 746 mm. $\text{N} = 9.7$.

$\text{C}_6\text{H}_{11}\text{O}_3\text{N}$ requires $\text{C} = 49.6$; $\text{H} = 7.6$; $\text{N} = 9.7$ per cent.

Methoxyl estimation: 0.1751 gave no AgI. $\text{MeO} = 0$.

N-Methyl estimation: 0.1751 ,, 0.2430 AgI. $\text{NMe} = 17.2$.

$\text{C}_5\text{H}_8\text{O}_3\text{N} \cdot \text{CH}_3$ requires $\text{NMe} = 20.0$ per cent.

* Dried at 105°.

The acid decomposes with effervescence at 242° , possesses little if any taste, is acid to litmus, but cannot be titrated, is not hygroscopic, and is optically active.

The specific rotatory power was determined in water of (a) a specimen of the acid crystallised from alcohol and containing $\text{H}_2\text{O}=5.13$, and (b) a specimen crystallised from water and containing $\text{H}_2\text{O}=10.8$ per cent.:

(a) $c=4.9910$, $l=1\text{-dcm.}$, $\alpha_D -4.02^{\circ}$; $[\alpha]_D -80.5^{\circ}$ or $[\alpha]_D -84.9^{\circ}$ for the anhydrous substance.

(b) $c=5.2300$, $l=1\text{-dcm.}$, $\alpha_D -3.98^{\circ}$; $[\alpha]_D -76.2^{\circ}$ or $[\alpha]_D -85.4^{\circ}$ for the anhydrous substance.

It gives a strong pyrrole reaction, and dissolves copper oxide with the formation of a copper salt. A quantity (0.2 gram) of the substance was dissolved in water, and the solution boiled for several hours with an excess of powdered copper oxide, the excess of copper oxide filtered off, and the filtrate concentrated. Blue prisms separated, which were dried on a porous tile, washed with 70 per cent. alcohol, and dried in the air:

0.1021 lost 0.0200 at 110° . $\text{H}_2\text{O}=19.6$.

$\text{C}_{12}\text{H}_{20}\text{O}_6\text{N}_2\text{Cu}, 4\text{H}_2\text{O}$ requires $\text{H}_2\text{O}=17.0$; $\text{C}_{12}\text{H}_{20}\text{O}_6\text{N}_2\text{Cu}, 5\text{H}_2\text{O}$ requires $\text{H}_2\text{O}=20.4$.

0.0669 (anhydrous salt) gave 0.0146 CuO. $\text{Cu}=17.4$.

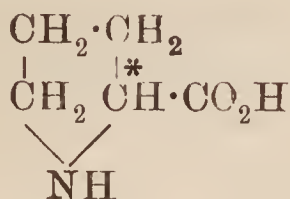
$\text{C}_{12}\text{H}_{20}\text{O}_6\text{N}_2\text{Cu}$ requires $\text{Cu}=18.1$ per cent.

Constitution of the Acid from Croton gubouga Bark.

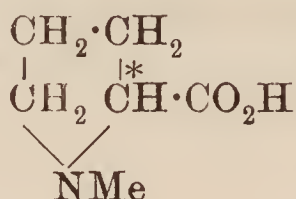
The evidence already given indicates that the substance is a 4-hydroxy-1-methylpyrrolidine-2-carboxylic acid (4-hydroxyhygric acid). Two such compounds have been synthesised by Leuchs and Felser (*Ber.*, 1908, **41**, 1726), namely, two optically inactive forms of 4-hydroxy-1-methylpyrrolidine-2-carboxylic acid. A comparison of the principal properties of these acids with that from *C. gubouga* bark is given in the following table:

	Formula.	$[\alpha]_D$.	M. p.	Reaction.	Taste.
Acid from Croton bark	$\text{C}_6\text{H}_{11}\text{O}_3\text{N}$	-85.4°	242°	faintly acid.	little or no taste.
a - 4 - Hydroxy - 1 - methylpyrrolidine-2-carboxylic acid.....	$\text{C}_6\text{H}_{11}\text{O}_3\text{N}$	inactive.	$207-208^{\circ}$	neutral.	marked sweet taste
b - 4 - Hydroxy - 1 - methylpyrrolidine-2-carboxylic acid	$\text{C}_6\text{H}_{11}\text{O}_3\text{N}$	inactive.	$226-227^{\circ}$	faintly acid.	sweetish insipid taste

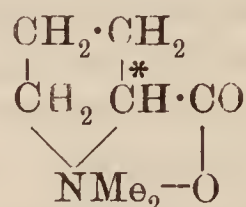
Comparison of the specific rotations of the closely related pyrrolidine derivatives indicates that in all probability this acid from Croton bark is 4-hydroxyhygric acid (γ -hydroxy-*N*-methylproline):



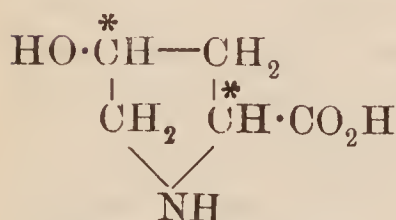
l-Proline (natural)
(Fischer), $[\alpha]_D -77.4^\circ$.



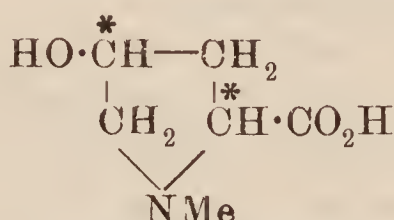
Hygric acid; active form does not appear to have been isolated.



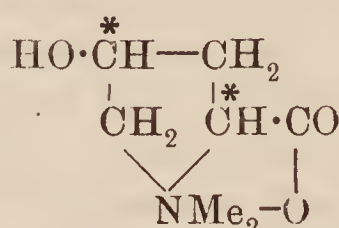
l-Stachydrine (natural),
 $[\alpha]_D$ of hydrochloride
 -26.5° (Yoshimura
and Trier).



l-Hydroxyproline
(Fischer), $[\alpha]_D -81.1^\circ$
(natural) (Leuchs
and Brewster),
 $[\alpha]_D -76.3^\circ$
(synthetic).



Formula suggested
for acid from Croton
bark, $[\alpha]_D -85.4^\circ$
(natural).



Betonicine	Turicine
hydrochloride,	(natural),
$[\alpha]_D -24.79^\circ$	hydrochloride
(natural);	$[\alpha]_D +24.65^\circ$.
hydrochloride,	
$[\alpha]_D -24.1^\circ$	
(synthetic).	

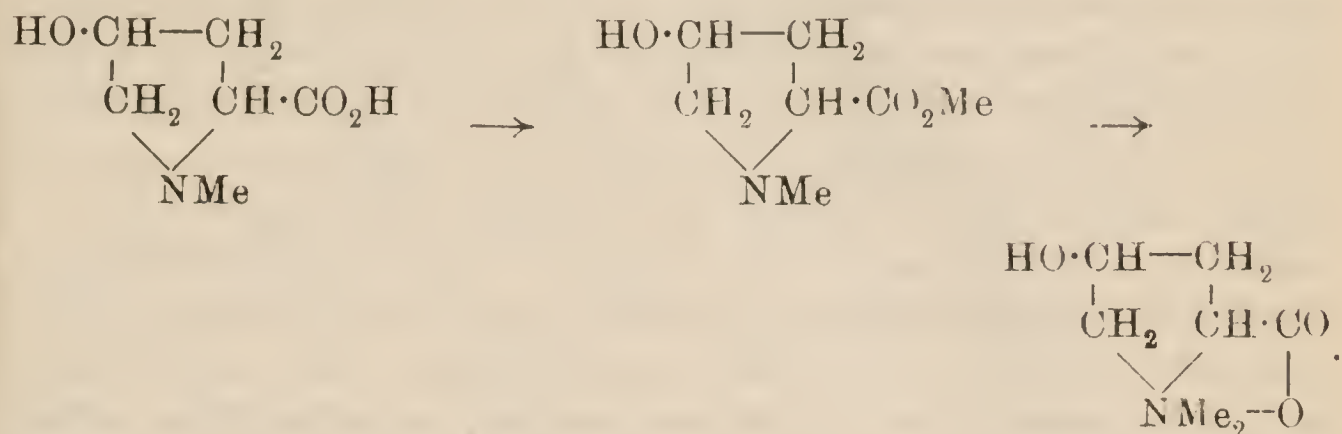
(Küng and Trier).

Leuchs and Brewster (*Ber.*, 1913, **46**, 986) have synthesised *l*-hydroxyproline, and Küng (*Zeitsch. physiol. Chem.*, 1913, **85**, 217) on methylating this substance obtained a mixture of the betaines, betonicine and turicine. If, therefore, the acid from *Croton gubouga* bark is in reality 4-hydroxyhygric acid it should in like manner, on methylation, give betonicine and turicine. Küng's method of methylation, with slight modification, was adopted, and resulted in the production of a mixture of betonicine and turicine, thus proving the acid to be 4-hydroxyhygric acid.

Küng (*loc. cit.*) has pointed out that turicine and betonicine are not enantiomorphs. When *l*-hydroxyproline or *l*-hydroxyhygric acid is methylated, using methyl iodide and alkali, it is probable that racemisation occurs and that one of the carbon atoms only, namely, that attached to the carboxyl group, is concerned in the racemisation. It will be interesting to see whether optically active hygric acid, which so far does not appear to have been obtained, and will only possess one asymmetric carbon atom, will yield on methylation two stereoisomeric betaines.

It seemed possible that methylation of the hydroxyhygric acid might be accomplished without racemisation if the use of alkali were avoided, and so evidence might be secured as to which of the

betaines, betonicine or turicine, corresponds with *l*-hydroxyproline and 4-hydroxyhygric acid. It was hoped that by passing hydrogen chloride into boiling methyl alcohol containing 4-hydroxyhygric acid the methyl ester would first be formed, and would pass into the corresponding betaine, thus:



It is probable that the ester was formed, but was rapidly hydrolysed, since on treating the hydrochloride with silver oxide the original 4-hydroxyhygric acid was recovered unchanged.

Methylation of the Acid.

A preliminary experiment was carried out, using 1 gram of the acid, which was dissolved in a mixture of 2 c.c. of water and 20 c.c. of methyl alcohol. Five c.c. of a solution of 6 grams of potassium hydroxide in 100 c.c. of methyl alcohol, and a like quantity of a solution of methyl iodide in methyl alcohol (3 grams in 20 c.c.), were added alternately 1 c.c. at a time. As the solution remained alkaline, a further 5 c.c. of the methyl iodide solution were added, and the mixture boiled on a water-bath for half an hour. One c.c. of methyl iodide was then added and sufficient methyl-alcoholic potassium hydroxide to render the liquid alkaline. The solution was boiled for about twenty minutes and made alkaline, again boiled for five minutes and made alkaline, and the operation repeated until the alkalinity persisted. The alcohol was distilled off, the residue dissolved in water, the solution made slightly acid with hydrochloric acid, and boiled with excess of silver chloride. The silver iodide and excess of silver chloride were filtered off, and the filtrate evaporated to dryness under diminished pressure. The residue was treated with absolute alcohol and again evaporated to dryness. The dry residue was extracted with five small quantities of boiling absolute alcohol; the first three of which removed all but traces of the hydrochlorides of the betaines. The alcohol was distilled off and the rotation of the residue determined, using water as solvent ($c=6.4275$, $l=1\text{-dcm.}$, $\alpha_D + 0.075^\circ$; $[\alpha]_D + 1.2^\circ$).

This result indicated that the methylation had proceeded as expected, and that a mixture of turicine and betonicine hydrochlorides in about equal amounts had been produced.

Küng and Trier (*loc. cit.*) pointed out the difficulty of separating turicine and betonicine by fractional crystallisation of their hydrochlorides, and recommended for this purpose the free bases. This the authors are able to confirm, since on dissolving the mixed hydrochlorides having $[\alpha]_D + 1.2^\circ$ in absolute alcohol, concentrating and allowing to crystallise, 0.667 gram of a mixture of rosettes of needles, and rosettes of plates was obtained which gave $[\alpha]_D + 3^\circ$ ($c = 3.335$, $l = 1\text{-dcm.}$, $\alpha_D + 0.10^\circ$), and on further recrystallisation a mixture of crystals amounting to 0.456 gram and having $[\alpha]_D + 5.0^\circ$ ($c = 2.280$, $l = 1\text{-dcm.}$, $\alpha_D + 0.115^\circ$) was obtained. The various solutions were united, the alcohol was removed by distillation under diminished pressure, and the free bases were liberated by treating the aqueous solution with excess of silver oxide. The silver chloride and excess of silver oxide were filtered off, the filtrate was concentrated, absolute alcohol added, and the solution again concentrated, this operation being repeated until crystals separated out on cooling. 0.137 Gram of substance crystallised in long prisms, which had a sweet taste, decomposed at 250° with frothing, and gave $[\alpha]_D + 21.2^\circ$ ($c = 2.6400$, $l = 1\text{-dcm.}$, $\alpha_D + 0.58^\circ$).

Five grams of the acid were then methylated as described above with slight modifications. The same proportions of methyl iodide, methyl-alcoholic potassium hydroxide and acid were used, but the solutions were more concentrated. The alcoholic solution of the mixed hydrochlorides from the extraction of the dried mixture of potassium chloride and betaine hydrochlorides was kept overnight to separate as much potassium chloride as possible. When the hydrochlorides had been converted into bases by treating their aqueous solution with silver oxide and the silver chloride and undissolved excess of silver oxide removed by filtration, hydrogen sulphide was passed through the solution of the bases to remove any silver in solution. The solution of the betaines was concentrated to low bulk under diminished pressure, alcohol added, and the solution again concentrated; this operation was repeated until crystallisation set in on cooling. From the mother liquor two further crops were obtained on concentration.

Crop I consisted of nearly pure turicine, amounting to 1.7 grams. The air-dried substance was examined polarimetrically in water:

$$c = 2.5330, l = 1\text{-dcm.}, \alpha_D + 0.87^\circ; [\alpha]_D + 34.3^\circ.$$

On recrystallisation until the optical rotation was constant, the value $[\alpha]_D + 40.9^\circ$ was obtained for the anhydrous substance.

Crop II weighed 1.2 grams and was a mixture:

$$c = 2.5840, l = 1\text{-dcm.}, \alpha_D - 0.48^\circ; [\alpha]_D - 18.6^\circ.$$

Crop III, weighing 1.06 grams, was also a mixture:

$$c = 2.6180, l = 1\text{-dcm.}, \alpha_D - 0.41^\circ; [\alpha]_D - 15.7^\circ.$$

Crops II and III were united, converted into hydrochlorides, dissolved in absolute alcohol, and the solution was concentrated, when 1.45 grams of nearly pure betonicine hydrochloride crystallised out:

$$c = 3.3765, l = 1\text{-dcm.}, \alpha_D - 0.75^\circ; [\alpha]_D - 22.2^\circ.$$

As it was found difficult to remove all traces of potassium chloride from the betonicine hydrochloride, and it was not possible to obtain a higher value than $[\alpha]_D - 22.9^\circ$ on recrystallising this particular specimen, a further methylation of the acid was tried with good results, using sodium hydroxide instead of potassium hydroxide; with this difference, 3.9 grams of the acid were methylated as in the previous experiment; 1.2731 grams of crude turicine were obtained as a first crop:

$$c = 6.3655, l = 1\text{-dcm.}, \alpha_D + 2.25^\circ; [\alpha]_D + 35.3^\circ \text{ for the anhydrous substance.}$$

The bases in the mother liquor were converted into hydrochlorides, and crystallised from absolute alcohol; 1.322 grams of nearly pure betonicine hydrochloride were obtained, having $[\alpha]_D - 22.7^\circ$ ($c = 6.6100, l = 1\text{-dcm.}, \alpha_D - 1.50^\circ$). This was recrystallised until its optical rotation remained constant, the highest reading being $[\alpha]_D - 24.8^\circ$ ($c = 3.5900, l = 1\text{-dcm.}, \alpha_D - 0.89^\circ$).

The bases in the mother liquor from the betonicine hydrochloride ($[\alpha]_D - 22.7^\circ$) were regenerated by treatment with silver oxide. On crystallisation from alcohol a further 0.4012 gram having $[\alpha]_D + 4.0^\circ$ ($c = 2.0060, l = 1\text{-dcm.}, \alpha_D + 0.08^\circ$) was obtained.

The formation of a mixture of turicine and betonicine by the methylation of the acid from *Croton gubouga* bark leaves no doubt that the acid is 4-hydroxyhygric acid, as formulated on p. 928.

Properties of Turicine.

Turicine crystallises from alcohol in flat prisms containing one molecule of water of crystallisation, which it rapidly loses in a vacuum desiccator. It is neutral to litmus, is not hygroscopic, has a sweet taste, and gives an intense pyrrole reaction. The anhydrous substance decomposes with frothing at 260° , as did a specimen kindly supplied by Prof. A. Küng; the decomposition point was not depressed on mixing the two specimens. The hydrated substance commenced to melt at about 249° , but finally decomposed with frothing at 256° . Prof. Küng's specimen, and a mixture of the

two, behaved in the same way. (Found, $\text{H}_2\text{O}=10.59$; $\text{C}_7\text{H}_{13}\text{O}_3\text{N}, \text{H}_2\text{O}$ requires $\text{H}_2\text{O}=10.17$. Found, $\text{C}=52.7$; $\text{H}=8.3$. $\text{C}_7\text{H}_{13}\text{O}_3\text{N}$ requires $\text{C}=52.8$; $\text{H}=8.2$ per cent.)

The specific rotations of three specimens of the anhydrous substance were determined in water:

- I. $c=1.8065$, $l=1\text{-dcm.}$, $\alpha_D + 0.75^\circ$; $[\alpha]_D + 41.5^\circ$.
- II. $c=1.3950$, $l=1\text{-dcm.}$, $\alpha_D + 0.57^\circ$; $[\alpha]_D + 40.9^\circ$.
- III. $c=2.0980$, $l=1\text{-dcm.}$, $\alpha_D + 0.85^\circ$; $[\alpha]_D + 40.5^\circ$.

Küng and Trier give $[\alpha]_D + 36.26^\circ$ for the hydrated betaine corresponding with $[\alpha]_D + 40.4^\circ$ for the anhydrous substance.

Turicine Hydrochloride.—This was prepared from the pure base. When crystallised rapidly from absolute alcohol it separated in needles, but when allowed to crystallise slowly, six-sided tablets were obtained. It is acid to litmus, and decomposes with frothing at 224° ; Küng and Trier give 222° and 223° as the melting and decomposing point. Its specific rotation was determined in water. $c=2.8000$, $l=1\text{-dcm.}$, $\alpha_D + 0.72^\circ$; $[\alpha]_D + 25.7^\circ$. Küng and Trier give $[\alpha]_D + 24.65^\circ$, and state that turicine is not hygroscopic, but the authors are of the opinion that it is slightly hygroscopic.

Turicine aurichloride was obtained by adding gold chloride solution to a concentrated aqueous solution of turicine hydrochloride. The crystals, which separated rapidly, were collected, dissolved in hot water, and the solution was allowed to cool, when the double chloride crystallised in clusters of yellow prisms. The decomposition point was determined in the same bath with a specimen of turicine aurichloride kindly supplied by Prof. Küng, and a mixture of the two specimens; the decomposition with frothing occurred in each case at $230\text{--}232^\circ$. Küng and Trier give the melting and decomposing point as 232° . (Found, $\text{Au}=39.0$; $\text{C}_7\text{H}_{13}\text{O}_3\text{N}, \text{HAuCl}_4$ requires $\text{Au}=39.5$ per cent.)

Properties of Betonicine.

The free base was obtained from the pure hydrochloride by treating with silver oxide. It crystallises anhydrous from alcohol in short, four-sided, truncated pyramids, is more readily soluble in alcohol than turicine, has a sweet taste, is neutral to litmus, and gives an intense pyrrole reaction. Küng and Trier state that it is not hygroscopic, and that it melts and decomposes at $243\text{--}244^\circ$; the purest specimen obtained by the authors was slightly hygroscopic and decomposed with frothing at 252° . (Found, $\text{C}=52.7$; $\text{H}=8.5$. $\text{C}_7\text{H}_{13}\text{O}_3\text{N}$ requires $\text{C}=52.8$; $\text{H}=8.2$ per cent.) The specific rotation was determined in water:

$$c=3.5050, l=1\text{-dcm.}, \alpha_D - 1.23^\circ; [\alpha]_D - 35.1^\circ.$$

Küng and Trier give $[\alpha]_D - 36.6^\circ$.

Betonicine hydrochloride crystallises from absolute alcohol in needles or prisms, which, after drying at 105° , decompose with frothing at 227° ; a specimen supplied by Prof. Küng, which was slightly coloured, after drying at 105° , decomposed with frothing at 224° ; a mixture of the two specimens decomposed at an intermediate temperature. Küng and Trier give the melting and decomposing point as $222-223^\circ$. The hydrochloride is not hygroscopic and is acid in reaction. The specific rotatory power was determined in water:

$$c = 3.5900, l = 1\text{-dm.}, \alpha_D = 0.89^\circ; [\alpha]_D = 24.8^\circ.$$

Küng and Trier give $[\alpha]_D = 24.79^\circ$ for natural betonicine hydrochloride, and Küng $[\alpha]_D = 24.1^\circ$ for his synthetic product.

Betonicine Aurichloride.—To a concentrated solution of betonicine hydrochloride a solution of gold chloride was added. There was no immediate separation of crystals as in the case of turicine hydrochloride. The solution was accordingly concentrated and, on cooling, four-sided, yellow plates crystallised out. When redissolved in hot water and kept, clusters of yellow tablets were obtained. The substance decomposed with frothing at $230-232^\circ$, the same temperature as a specimen supplied by Prof. Küng, and a mixture of the two specimens also decomposed at this point. (Found, $\text{Au} = 39.2$. $\text{C}_7\text{H}_{18}\text{O}_3\text{N}, \text{HAuCl}_4$ requires $\text{Au} = 39.5$ per cent.)

The authors desire to take this opportunity of thanking Prof. Küng for his kindness in supplying them with specimens of turicine, turicine aurichloride, betonicine hydrochloride, and betonicine aurichloride for comparison.

WELLCOME CHEMICAL RESEARCH LABORATORIES,
LONDON, E.C. 1.

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